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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,079	02/16/2000	Gail M. Clinton	49321-16	5713

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
12/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/506,079	CLINTON ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-10,18-20 and 38-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *45-49* is/are allowed.

6)☒ Claim(s) *1,2,18-20,42 and 43* is/are rejected.

7)☒ Claim(s) *3,8-10,38-41 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 9/24/2007 is acknowledged.

Claims 1-3, 8-10, 18-20 and 38-49 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections Withdrawn:

3. The objection to claims 44, 45, 48 and 49 for phrases such as "polypeptide consisting of SEQ ID NO: 14" or "polypeptide comprises SEQ ID NO: 15", for example, is withdrawn in view of the amendments to the claims.

4. The rejection of claims 1-3, 8-10, 18-20, 38-44, 46-48 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

5. The rejection of claims 1, 18, and 19 remain rejected under 35 U.S.C. 102(a) as being anticipated by Doherty-I (Proc. Natl. Acad. Sci., USA, 96: 10869-10874, 1999, September; of record) is withdrawn in view of the amendment to the claims.

Applicants have added the limitation that the polypeptide comprises with respect to SEQ ID NO: 14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO: 19, the position 2 Ser; with respect to SEQ ID NO: 20, the position 5 Pro; with respect to SEQ ID NO: 21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO: 22, the position 16 Gln; with respect to SEQ ID NO: 23, the position 18 Leu; with respect to SEQ ID NO: 24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO: 25, the position 36 Ile; with respect to SEQ ID NO: 26, the position 54 Arg; with respect to SEQ ID NO: 27, the position 64 Leu; or with respect to SEQ ID NO: 28, both the position 6 Pro and the position 73 Asn. This limitation is interpreted to mean that the polypeptide, to the extent that it comprises fragments of about 50 to 79 contiguous residues in length from SEQ ID NOS: 14, and 19-28, comprises those fragments that encompass, for example with respect to SEQ ID NO: 19, position 6 of the amino acid sequence of SEQ ID NO: 19, and that the amino acid at position 6 is a proline (Pro). In view of this interpretation, the rejection over Doherty-I is withdrawn, because the sequence of Herstatin taught in Doherty does not comprise any of the sequences recited in the claims. However, this rejection may be reinstated if applicants amend the claims to remove the limitation specifying the structure of the fragments (comprising certain positions, and where the positions have certain specific residues).

6. The rejection of claims 1, 18, 19 and 20 under 35 U.S.C. 102(e) as being anticipated by Doherty-II (U.S. 6,414,130; published Jul. 2, 2002; effective filing date Jan. 20, 1999; of record) is withdrawn in view of the amendments to the claims.

Applicants have added the limitation that the polypeptide comprises with respect to SEQ ID NO: 14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO: 19, the position 2 Ser; with respect to SEQ ID NO: 20, the position 5 Pro; with respect to SEQ ID NO: 21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO: 22, the position 16 Gln; with respect to SEQ ID NO: 23, the position 18 Leu; with respect to SEQ ID NO: 24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO: 25, the position 36 Ile; with respect to SEQ ID NO: 26, the position 54 Arg; with respect to SEQ ID NO: 27, the position 64 Leu; or with respect to SEQ ID NO: 28, both the position 6 Pro and the position 73 Asn. This limitation is interpreted to mean that the polypeptide, to the extent that it comprises fragments of about 50 to 79 contiguous residues in length from SEQ ID NOS: 14, and 19-28, comprises those fragments that encompass, for example with respect to SEQ ID NO: 19, position 6 of the amino acid sequence of SEQ ID NO: 19, and that the amino acid at position 6 is a proline (Pro). In view of this interpretation, the rejection over Doherty-I is withdrawn, because the sequence of Herstatin taught in Doherty does not comprise any of the sequences recited in the claims. However, this rejection may be reinstated if applicants amend the claims to remove the limitation specifying the structure of the fragments (comprising certain positions, and where the positions have certain specific residues).

7. The provisional rejection of claims 1, and 18-20 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 8-10, 18-20, 27, 28, 29, and 30 of copending Application No. 09/234,208 is withdrawn in view of the amendments to the claims.

Applicants have added the limitation that the polypeptide comprises with respect to SEQ ID NO: 14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO: 19, the position 2 Ser; with respect to SEQ ID NO: 20, the position 5 Pro; with respect to SEQ ID NO: 21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO: 22, the position 16 Gln; with respect to SEQ ID NO: 23, the position 18 Leu; with respect to SEQ ID NO: 24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO: 25, the position 36 Ile; with respect to SEQ ID NO: 26, the position 54 Arg; with respect to SEQ ID NO: 27, the position 64 Leu; or with respect to SEQ ID NO: 28, both the position 6 Pro and the position 73 Asn. This limitation is interpreted to mean that the polypeptide, to the extent that it comprises fragments of about 50 to 79 contiguous residues in length from SEQ ID NOS: 14, and 19-28, comprises those fragments that encompass, for example with respect to SEQ ID NO: 19, position 6 of the amino acid sequence of SEQ ID NO: 19, and that the amino acid at position 6 is a proline (Pro). In view of this interpretation, the rejection over Doherty-I is withdrawn, because the sequence of Herstatin taught in Doherty does not comprise any of the sequences recited in the claims. However, this rejection may be reinstated if applicants amend the claims to remove the limitation specifying the structure of the fragments (comprising certain positions, and where the positions have certain specific residues).

Claim Rejections Maintained:

8. Claims 1, 2, 18-20, 42 and 43 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment filed 9/24/2007 introduces new matter into the specification as originally filed.

Applicants' amendments to the claims and arguments have been carefully considered, but fail to persuade.

Applicants have replaced the limitation "wherein the fragments comprise the respective polymorphic amino acid positions of the corresponding SEQ ID NOS: 14 and 19-28" or "polymorphism-comprising fragments" with the limitation that the polypeptide comprises with respect to SEQ ID NO: 14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO: 19, the position 2 Ser; with respect to SEQ ID NO: 20, the position 5 Pro; with respect to SEQ ID NO: 21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO: 22, the position 16 Gln; with respect to SEQ ID NO: 23, the position 18 Leu; with respect to SEQ ID NO: 24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO: 25, the position 36 Ile; with respect to SEQ ID NO: 26, the position 54 Arg; with respect to SEQ ID NO: 27, the position 64 Leu; or with respect to SEQ ID NO: 28, both the position 6 Pro and the position 73 Asn. This limitation is interpreted to mean that the polypeptide, to the extent that it comprises fragments of about 50 to 79 contiguous residues in length from SEQ ID NOS: 14, and 19-28, comprises those fragments that encompass, for example with respect to SEQ ID NO: 19, position 6 of the amino acid sequence of SEQ ID NO: 19, and that the amino acid at position 6 is a proline (Pro).

Additionally, applicants present the following arguments. Applicants assert that the ECDIIIa variant containing polypeptides, both comprising the ECDIIIa or sub fragments thereof,

is indeed encompassed within the original specification teachings. Applicants state that the claims have been amended to delineate the variant residues, including sub-fragment residues. Support for the new claims is asserted by applicant to be found in Table I or the originally-filed specification and original claim 27 reciting "ECDIIIa variant sequence". Applicants also point to the following passage in the specification :"[t]his result demonstrates that in the human population there are several variants in the intron-8 encoded domain that could lead to altered biochemical and biological properties among ECDIIIa-containing protein variants" (page 32, ll.21-23). Additionally, applicants point to page 14, ll. 6-8: "[f]or the production of antibodies, various host animals may be immunized by injection with e.g., polyhistidine-tagged ECDIIIa variants or mutants of the ECDIIIa region", and to page 17, ll. 19-20: "PCR, or reverse transcription can be utilized to identify nucleotide variation within the ECDIIIa domain." Applicants also refer to a declaration made by Dr. Gail Clinton (19 April 2003), in which she stated: "[t]he discovery of these novel polymorphisms was precisely the reason that the present application was filed. The Herstatin sequence of the earlier U.S. patent application (09/234,208) was already disclosed and claimed in that application, and it was the primary purpose of the present application to claim additional polymorphisms, while not claiming the previously claimed Herstatin." Applicants also state that the specification discloses new polymorphic variants and ECDIIIa variant fragments of about 50 to about 79 amino acids and that no new matter has been added.

In response, it is noted that the rejection of the claims in not based on the finding that the specification fails to teach polypeptides that comprise the fragments as recited in the claims. It is that the new matter issue is due to the fact that the current set of claims is an attempt to carve out

a patentable portion of what is broadly disclosed in the specification. The specification discloses the sequences that are the polymorphisms of the previously disclosed Herstatin sequence. The specification contemplates polypeptides that comprise any 50 to 79 contiguous amino acids from these sequences, where the polypeptides bind to the ECD of Her-2 with an affinity binding constant of 10^8M^{-1}. However, the specification fails to provide support for the limitation that the fragments must comprise the residues that are different from the previously disclosed Herstatin sequence. While the claims do not explicitly recite a negative limitation, by reciting limitations that require the claimed polypeptides that comprise a specific residue from a sequence, the claims are excluding fragments of 50 to 79 amino acids in length that are the same as fragments of 50 to 79 amino acids in length that have already been disclosed in the prior art (e.g. U.S. 6,414,130). Thus, the claims imply a negative limitation or an exclusionary proviso. The MPEP (2173.05(i)) states that any negative limitation or exclusionary proviso must have basis in the original disclosure. Applicants' arguments, while presenting evidence that the claimed polypeptides with respect to polypeptides comprising the recited fragments are *encompassed* by the teachings of the specification, fail to provide support for a new genus of polypeptides that has been carved away from the originally disclosed genus. Therefore, the rejection is maintained for the reasons of record.

Claims 3, 8-10, 39, 44, 46-48 are not included in this rejection because the claims are either drawn to a polypeptide comprising the entire sequence of any of SEQ ID NOS: 14 and 19-28, or the claims are drawn to fragments of a larger sequence that inherently includes all of any one of SEQ ID NOS: 14 and 19-28 as the C-terminal 79 contiguous amino acids (For example, the sequence of the C-terminal 79 contiguous amino acids of SEQ ID NO: 15 are the same as the

sequence of SEQ ID NO: 14. In claim 8, which recites that the fragments are of about 80 to 419 contiguous residues in length, wherein the C-terminal 79 contiguous amino acids are present, the entire sequence of any one of SEQ ID NOS: 14 and 19-28 is included within each of the claimed polypeptides).

New Grounds:

9. Claims 1, 8-10, 18, 38, and 39 are objected to for typographical errors. In claims 1, 8, 18, 38 and 39 the term "Ala" has been typed as "Alu". In claims 8, 18 and 39, for SEQ ID NO: 38, the position "73" is referred to when it should be position "413". Claims 9 and 10 are included in this objection because they depend from claim 8.

Conclusion

Claims 1, 2, 18-20, 42 and 43 are rejected. Claims 3, 40, 41 and 44 are objected to for depending from rejected claims. Claims 8, 38 and 39 are objected to for the reasons given above, but are otherwise allowable, as are claims that depend from those claims (claims 9, 10). Claims 45-49 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
December 4, 2007

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER